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PATENT ABSTRACTS OF JAPAN

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**(54) COMPOSITION FOR PERCUTANEOUS DELIVERY SYSTEM CONTAINING
NONSTEROIDAL ANTIINFLAMMATORY AGENT AS ACTIVE COMPONENT**

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain a composition for a percutaneous delivery system having excellent skin-penetration effect and exhibiting high analgesic and antiinflammatory effect by dispersing a nonsteroidal antiinflammatory agent in a specific polymer base.

SOLUTION: A nonsteroidal antiinflammatory agent such as a propionic acid derivative is dispersed in a non-polar tacky polymer base. The polymer base is preferably free from functional group such as natural rubber, butyl rubber, polyisobutylene and polystyrene. The total amount of the nonsteroidal antiinflammatory agent is 0.5-30wt.% based on the total weight of the composition excluding the releasing paper and the backing layer. The propionic acid derivative is preferably ketoprofen, flurbiprofen, loxoprofen and pranoprofen, especially ketoprofen. The composition may be further incorporated with one or more compounds selected from a dissolution assistant, an absorbefacient, a plasticizer, a tackifier and an antioxidant.

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CLAIMS

[Claim(s)]

- [Claim 1] The constituent characterized by distributing 1 or this antiphlogistic beyond it which is the constituent of the endermic delivery system containing the non-steroidal anti-inflammatory drug and macromolecule basis as an active ingredient, and was chosen out of the propionic-acid derivative in a nonpolar tackiness macromolecule basis.
- [Claim 2] The constituent of the endermic delivery system according to claim 1 characterized by a nonpolar tackiness macromolecule basis being a nonpolar polymeric material without a functional group.
- [Claim 3] The constituent of the endermic delivery system according to claim 1 or 2 characterized by choosing the nonpolar tackiness macromolecule basis without a functional group from natural rubber, isobutylene isoprene rubber, a polyisobutylene, polystyrene, a polyisoprene, a polybutadiene, polyethylene/butylene, polyethylene / propylenes, those copolymers, and other polymers that have the same solubility constant.
- [Claim 4] The constituent of the endermic delivery system according to claim 1 characterized by the total amount of a non-steroidal anti-inflammatory drug being 0.5 – 30% of the weight of the domain of the AUW of the constituent except ***** and the tooth-back layer.
- [Claim 5] The constituent of the endermic delivery system according to claim 1 by which a propionic-acid derivative is characterized by being chosen from ketoprofen, a ***** pro Foehn, a ***** pro Foehn, and a ***** pro Foehn.
- [Claim 6] The constituent of the endermic delivery system of the claim 1–5 characterized by a propionic-acid derivative being ketoprofen given in any one term.
- [Claim 7] The constituent of the endermic delivery system according to claim 1 characterized by including one or two additives or more which were chosen from the group which a constituent becomes from a solubilizing agent, an absorption adjuvant, a **** agent, a tackifier, and an anti-oxidant further.
- [Claim 8] A solubilizing agent or an absorption adjuvant is 50mg/ml to a fatty acid, fatty acid ester, a fatty alcohol, a propylene glycol and its fatty acid ester, ethylene glycol monoethyl ether, and an active ingredient. Constituent of the endermic delivery system according to claim 7 characterized by being one or two mixture or more which were chosen from the group which consists of the arbitrary lipophilic property solvents which have large solubility.
- [Claim 9] The constituent of the endermic delivery system according to claim 7 or 8 characterized by the content of a solubilizing agent and an absorption adjuvant being 0.01 – 35% of the weight of the domain of the total amount of the constituent except ***** and the tooth-back layer.
- [Claim 10] The constituent of the endermic delivery system according to claim 7 characterized by being chosen from the group which a **** agent becomes from a polybutene, a paraffine wax, petroleum oil, a coal tar distillate, rosin, a chlorinated hydrocarbon, ester, and the ***** acid ester with a long aliphatic side chain.
- [Claim 11] The constituent of the endermic delivery system according to claim 7 or 10 characterized by the content of a **** agent being 0.1 – 60% of the weight of the domain of the total amount of the constituent except ***** and the tooth-back layer.
- [Claim 12] The constituent of the endermic delivery system according to claim 7 characterized

by being chosen from the group which a tackifier becomes from a rosin and its derivative, hydrocarbon-resin, aromatic resin, and miscibility resin, an alkylation phenol, a terpene resin, terpene phenol resin, rosin ester, hydrogenation ester, and the polyisobutylene of low molecular weight.

[Claim 13] The constituent of the endermic delivery system according to claim 7 or 12 characterized by the content of a tackifier being 0.1 – 70% of the weight of the domain of the total amount of the constituent except ***** and the tooth-back layer.

[Claim 14] The constituent of the endermic delivery system according to claim 7 characterized by choosing the anti-oxidant from the group which consists of butylhydroxytoluene, butylhydroxyanisole, and a tocopherol.

[Claim 15] The constituent of the endermic delivery system according to claim 7 or 14 characterized by the content of an anti-oxidant being 0.001 – 5% of the weight of the domain of the total amount of the constituent except ***** and the tooth-back layer.

[Claim 16] The endermic delivery system by which it is the endermic delivery system by which the active ingredient according to claim 1 is distributed by the substrate layer of the gestalt of a matrix, or 1 or the additive beyond it according to claim 7 is further added by the substrate layer in addition to this active ingredient, this substrate layer was applied between ***** and the tooth-back layer, and this substrate layer was applied as multilayer structure of 2–5 layers as monolayer structure.

[Claim 17] The endermic delivery system according to claim 16 by which the active ingredient which is the steroid nature antiphlogistic is characterized by arbitrary 1 or the arbitrary layers beyond it distributing among multilayer substrate layers.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[The technical field to which invention belongs] this invention is a thing about the constituent of the endermic delivery system containing a non-steroidal anti-inflammatory drug like a propionic-acid derivative called ketoprofen. more specifically A nonpolar macromolecule is made to distribute the above non-steroidal anti-inflammatory drugs. Make the thermodynamic reactivity maximum-ize continuously, and when required, as a solubilizing agent or an absorption accelerator A fatty acid, Fatty acid ester, fatty-acid alcohol, a propylene glycol, propylene glycol fatty acid ester, It is related with the constituent for the improved endermic delivery system to which the skin transmittance of an active ingredient was made to increase using an oleic acid, olein alcohol, ethylene glycol monoethyl *****, or its mixture.

[0002]

[Description of the Prior Art] Ketoprofen is a non-steroidal anti-inflammatory drug which has the painkilling operation used for an arthritis, an osteoarthritis, muscular pain, etc. However, when ketoprofen is prescribed for the patient by taking orally, there is demerit which digestive trouble generates from many patients, and the biological half life is short and must usually prescribe for the patient three - four days. Especially, since an arthritis patient has to prescribe a medicine for the patient over a long period of time continuously, occurrence frequency of a side effect is high. There is the need of developing suitable routes of administration other than internal use from these side effects and inconvenient. Generally, digestive trouble can be prevented when an active ingredient is carried endermically. Moreover, since an active ingredient is continuously emitted at a fixed speed from macromolecule *****, the number of times of medication can be reduced. From the above-mentioned advantage, the endermic delivery system is applied in various medicines other than a non-steroidal anti-inflammatory drug. Although it has many advantages in which such an endermic delivery system avoids the first time transit effect of a liver further etc., since the skin as a biophylaxis mechanism has low transmittance to the medicine, **** is applied only to the medicine powerful in comparison.

[0003] Now, the medicine currently sold as an endermic delivery system has a scopolamine, nitroglycerin, clo *****, Foehn *****, nicotine, an estradiol, etc. These systems are roughly divided into the matrix type and the storage layer (reservoir) type. A matrix type makes a macromolecule matrix and a binder distribute a medicine, and a storage layer type is the format of adjusting exudation of a medicine using a control layer. The bigger demerit of an endermic delivery system is that the permeability of the activator object which passes the skin is quite low as it was explained above. Then, because of the development of these dosage forms, it is required to make permeability increase. It is concluded that it is quite important for it to be comparatively alike like ketoprofen and to make the permeability maximum-ize in the non-steroidal anti-inflammatory drug with the high amount used especially for the one day. The acrylic resin from which water absorption capacity is different is built with South Korean patent public presentation of No. 21137 [92 to] to multilayer structure, and the percutaneous absorption tablet which the maximum was made to melt a medicine in the adhesive layer in contact with the skin, and was manufactured is proposed. However, simply, the skin permeability of a medicine makes the solubility increase, and is not improved, and this South

Korean patent official report is not indicating the technique of maintaining the saturated concentration of a medicine continuously in the adhesive layer.

[0004] That is, the absorption process of the medicine which generally passes the skin happens by the simple diffusion. It is more like [although it is said that the medicine absorbed dose is generally proportional to the concentration gradient of a medicine / accuracy] the following formula. Fick By the principle, it is proportional to the chemical potential of a medicine.

Amount of the medicine penetrated per unit area with J:unit time among $J = \frac{D}{x} \frac{d\mu}{dx}$ formula;

μ : Chemical potential of a medicine;

x : Membranous thickness.

Moreover, the following relations are materialized between chemical potential and a thermodynamic reactivity.

Inside of a $\mu = \mu^* + RT \ln a$ formula, chemical potential in μ^* :reference condition.

R: Gas constant T:absolute-temperature a:thermodynamic reactivity.

Furthermore, the following relations are materialized between a thermodynamic reactivity and concentration.

γ is the activity coefficient among an $a = \gamma C$ formula, and C is concentration.

[0005] If medicine concentration is low, the activity coefficient will be set to 1 from the above-mentioned formula, and a straight-line relation is materialized between a thermodynamic reactivity and concentration. however, if this medicine concentration is alike to some extent and reaches, the activity coefficient will decrease and it will stop maintaining a straight-line relation In the case of the saturated solution, the thermodynamic reactivity of a medicine becomes the maximum, and the value at this time is 1. Therefore, in order to maximum-ize the permeability of a medicine, you have to maintain a saturated concentration continuously in the term which uses a tablet. Another mechanism by which a medicine penetrates the skin in addition to a simple diffusion is a transportation by the solvent. For this reason, the suitable selection of a solvent which has high skin permeability and the solubility of a medicine is needed.

[0006] In addition, conventionally, as an example which made the non-steroidal anti-inflammatory drug apply to a percutaneous absorption tablet, although the Japanese patent public presentation common of No. 233050 [seven to] is indicating the constituent of the external application part pasting agent which makes an active ingredient a non-steroidal anti-inflammatory drug and a muscle relaxant, it is not describing it about the effect change by the physical chemistry-property of the binder to use. Moreover, by the patent, although the constituent of the external application part pasting agent which makes a basis a powdered polyacrylic acid and a water soluble polymer is described, since the Japanese patent public presentation common of No. 135828 [six to] is not taking the thermodynamic reactivity of an active ingredient into consideration, it seldom expects high skin transmittance. On the other hand, WONO.93/04677 are describing that a styrene-isoprene-styrene copolymer can be used and L-menthol and the suitable mixture of a rosin-ester derivative can be used as the solvent or exudation accelerator of a non-steroidal anti-inflammatory drug as a macromolecule basis. However, some side effects of a skin stimulus are guided by L-menthol, and the curative effect of the constituent may be changed with the type of a tooth-back layer.

[0007]

[Problem(s) to be Solved by the Invention] In order that this invention may complement the above demerits, on the basis of the rationale by percutaneous absorption and the simple diffusion So that the percutaneous absorption of the active ingredient of the aforementioned non-steroidal anti-inflammatory drug may be promoted greatly and the new endermic delivery system which can raise a utilization factor in the living body may be developed Distribute a non-steroid nature medicine to the adhesive layer which makes a nonpolar macromolecule a basis, and as occasion demands, the solubility to the activator object is 50mg/ml or more, skin transmittance makes a solvent good in comparison lysis aid and an absorption adjuvant, and it

adds further. The purpose is in offering the constituent of the new endermic delivery system to which the percutaneous absorption of an active ingredient is made to increase remarkably. [0008]

[Means for Solving the Problem] This invention persons tried their best to develop the new endermic delivery system designed so that the utilization factor of an active ingredient in the living body might be promoted in the basis of the rationale by percutaneous absorption or the simple diffusion. Consequently, it was found out that the painkilling endermic delivery system which has the ideal physical characteristic of good skin tackiness, suitable internal cohesive force, and the good stability about an active ingredient can be offered at the same time the binder which makes a nonpolar macromolecule a basis had improved endermic absorption of an active ingredient by maximum-izing thermodynamic activity. this invention is characterized [the] by distributing one chosen as the nonpolar tackiness macromolecule basis out of the component of a propionic-acid derivative as an active ingredient in the constituent of the endermic delivery system which consists of making a macromolecule basis contain a non-steroidal anti-inflammatory drug, or the active ingredient which is the non-steroidal anti-inflammatory drug of the more than.

[0009]

[Embodiments of the Invention] It is as follows if this invention is explained in detail. Propionic-acid derivatives, such as ketoprofen, are one sort of a non-steroidal-anti-inflammatory drug, have comparatively high compatibility, therefore high solubility on the physical chemistry-property to the adhesives which make an acrylic macromolecule a basis, and have the inclination to **** to the inside of the acrylic macromolecule. Therefore, the exudation speed from an acrylic macromolecule becomes slow, and the amount of the medicine carried through the skin decreases. When applying an active ingredient to a macromolecule basis based on such a fault, in order to improve the skin transmission rate of this active ingredient, use of an absorption accelerator is needed. However, even when using a transparency accelerator simply, a limitation is in the effect and it is necessary to use the macromolecule basis of other modalities.

[0010] Therefore, in this invention, as a result of inquiring with the application of various kinds of components as a macromolecule basis unlike the former, if a nonpolar macromolecule basis is used, the thermodynamic reactivity of active ingredients, such as ketoprofen, will be maximum-ized, and the exudation speed from a macromolecule will be maximum-ized by the difference of the physical chemistry-property with a macromolecule basis. As a result, it was made to improve so that the absorption coefficient by endermic medication of a non-steroid nature medicine was not expected, and the high utilization factor in the living body was able to be obtained. As an example of the propionic-acid derivative which can be used in this invention, ketoprofen is begun and a ***** pro Foehn, a ***** pro Foehn, a ***** pro Foehn, etc. are used, for example. As a nonpolar macromolecule, the nonpolar polymeric material without a functional group is more desirable from the physical chemistry-property. As a nonpolar macromolecule basis which can be used in this invention, natural rubber, isobutylene isoprene rubber, a polyisobutylene, etc. polystyrene, a polyisoprene, a polybutadiene and polyethylene/butylene or polyethylene/propylenes, and those copolymers can be used, for example. In addition, the macromolecule shown above and the macromolecule to which a solubility constant is similar can also be used.

[0011] Moreover, although according to this invention a utilization factor in the living body is greatly increased by use of a nonpolar macromolecule as explained above If the solubility to an active ingredient is 50mg/ml or more and the skin transmittance of itself also adds a solvent good in comparison in addition to this in what should be surprised more It not only raises the solubility of a non-steroid nature medicine, but the transportation by the solvent can also raise the absorption coefficient of a medicine, and it can increase a utilization factor in the living body more. Thus, 1 or two or more things which were chosen from the group which consists of a fatty acid, fatty acid ester, a fatty alcohol, propylene ***** or its fatty acid ester, and ethylene glycol monoethyl ether as an example of the suitable solvent which can be used as a solubilizing agent and/or an absorption adjuvant are mentioned. In addition, the

solvent of the arbitrary lipophilic property which shows the solubility of 50mg/ml or more to an active ingredient can also be used.

[0012] In this invention, in order to increase a utilization factor in the living body more, the various absorption adjuvants which this technical field is sufficient as and are known can be added to a constituent. As an example of an above-mentioned absorption adjuvant, an alkyl sulfoxide, ***** (azone) and its derivative, a pyrrolidone and its derivative, non-ionicity and an ionic surfactant, a fatty acid, fatty acid ester, a urea and its derivative, alcohols, a glycol, etc. are mentioned. Moreover, a **** agent and a tackifier can be used according to the modality of macromolecule used. Although well-known arbitrary **** agents and tackifiers can be used for this invention by this technical field, the macromolecule and solubility constant by which a **** agent is used into a tablet must be similar. As an example of a plasticizer, a polybutene, a paraffine wax, petroleum oil, a coal tar distillate, rosin, a chlorinated hydrocarbon and ester, the phthalic ester that has a long aliphatic side chain are mentioned. A tackifier can also use the component known widely and rosin and its derivative, hydrocarbon-resin, aromatic resin, and resin mixture, an alkylation phenol, a terpene resin, terpene phenol resin, rosin ester, hydrogenation ester, the polyisobutylene of low molecular weight, etc. are mentioned as the example. Thus, the mixture of the component constituted by this invention is applied to an available tooth-back layer and available ***** in the commercial scene used for the manufacture of an endermic delivery system.

[0013] The amount of each component used by this invention is concretely explained by the following. The concentration domain of the propionic-acid derivative which is an active ingredient is 0.1 – 30% of the weight of the weight of a tooth-back layer and all the constituents except *****, and is 0.5 – 20 % of the weight preferably. If there are few contents of an active ingredient than 0.1%, it is hard to expect sufficient clinical effect, and even if it exceeds 30%, the clinical effect beyond it is not expectable. As a solubilizing agent and an absorption adjuvant, the concentration domain of the solvent to use is 0.01 – 35% of the weight of the weight of a tooth-back layer and all the constituents except *****, and can contain 0.1 – 15 % of the weight preferably. If the amount of solvents is less than 0.01%, when the improvement effect of skin transparency will exceed 35 % of the weight which is not enough, adhesion declines and the goods value is inferior. Although the concentration domain of a **** agent must adjust the amount pertinently with the property of a macromolecule basis, it is usually 0.1 – 60% of the weight of the weight of a tooth-back layer and all the constituents except *****, and is 1 – 40 % of the weight preferably. If the amount of a **** agent is less than 0.1 % of the weight, the flexibility of a macromolecule basis will be lost, and skin adherability will become incongruent if 60 % of the weight is exceeded.

[0014] Moreover, according to the modality of macromolecule basis to use, it is necessary to add a tackifier so that suitable adhesion may be offered. The concentration domain of a tackifier is 0.1 – 70% of the weight of the weight of a tooth-back layer and all the constituents except *****, and is 0.1 – 60 % of the weight preferably. If adhesion is inferior and it cannot stick on the skin well, if a tackifier is less than 0.1 % of the weight, and 70 % of the weight is exceeded, it is difficult, and removing from the skin may remain on the skin and it is unsuitable. Since the decomposition by oxidization of a macromolecule basis and an active ingredient is prevented, an available anti-oxidant can be added in the commercial scenes already known well, such as butylhydroxytoluene, butylhydroxyanisole, and a tocopherol. The concentration domain of an anti-oxidant is 0.001 – 5% of the weight of the weight of a tooth-back layer and all the constituents except *****, and is 0.01 – 2 % of the weight preferably. If there are few amounts of an anti-oxidant than 0.001 % of the weight, it is hard to expect sufficient antioxidation effect, and if 5% is exceeded, the antioxidation effect of the more than will not be seen.

[0015] It is made to become 100% of the weight about the whole using the macromolecule basis of a non-polarity besides the component explained above. If weight % of an adhesive macromolecule basis is too low, adhesion declines, and the storage capacity of an active ingredient becomes low and is not desirable. Therefore, in order to conquer this problem that is not desirable, and in order to attain the purpose of this invention, you should make the

weight proportion of a macromolecule basis increase. after mixing the component chosen by this invention, the mixture is shown in the drawing 1 and the drawing 2 -- as -- ***** (1) and (11) (13c) And a tooth-back layer (2) and (12) between -- monolayer ***** -- the laminated structure of 2-5 layers ***** -- applying -- a substrate layer (3) and (13a) (13b) It forms. When manufacturing by the multilayer structure which carried out the laminating, an active ingredient can be added only in a single layer and it can also put into many layers. [0016] How to form a substrate layer (3), (13a), (13b), and (13c) is more explained to a detail. The mixture of the selected component which it is going to apply is melted into aliphatic hydrocarbon and toluene, the halogenated solvents, or those mixture, or is heated and melted. The mixture is applied to ***** (1) by the thickness decided beforehand, and is imprinted to a tooth-back layer (2) after suitable xerensis. The mixture can also be again applied to a tooth-back layer (2) directly. When manufacturing by multilayer structure, above-mentioned operation can be repeated. In all cases, as shown in the drawing 1 and the drawing 2, ***** (1, 11) has adhered, and when using it, the opposite side of a tooth-back layer (2, 12) removes ***** (1, 11), and adheres to the skin. Thus, the gestalt of the final product of the endermic medication tablet manufactured by this invention consists of the structure which the substrate layer (3, 13a, 13b, 13c) of the macromolecule ***** gestalt in which the medicine or the medicine, and the suitable additive were contained minds between ***** (1, 11) and a tooth-back layer (2, 12). Hereafter, this invention is explained in detail based on an example. this invention is not limited by these examples.

[0017]

[Example 1] 3g ketoprofen and low molecular weight (molecular weight domains 40,000-60,000) The polyisobutylene of the grade of 60:40 mixture of interval molecular weight (molecular weight domain 1,000,000-1,500,000) was stirred until it melted liquid paraffin (28g and 14g), 1.5g propylene-glycol monochrome laurate, and 28mg butylhydroxytoluene in a hexane / toluene mixture and it melted completely. This mixture is applied to ***** it dries for 30 minutes at 50 degrees C, and thickness is 70 micrometers. It was made to become (layer A). By the same operation as layer A, all the components of the **** except ketoprofen were melted to the hexane. The mixture is applied to ***** it dries for 30 minutes at 50 degrees C, and thickness is 70 micrometers. It was made to become (layer B). By the same operation as layer B, all the components of layer B were melted except having used the polyisobutylene of the grade of 50:50 mixture of low molecular weight and interval molecular weight. The mixture is applied to ***** is dried for 30 minutes at 50 degrees C, and thickness is 70 micrometers. It was made to become (layer C). Layer C was imprinted with a roll to the tooth-back layer, and ***** was removed after that. Subsequently, the laminating of the layer B was carried out to up to layer C, and, subsequently the laminating of the layer A was carried out to up to layer B. ***** which has adhered on layer A was not removed until it used the product. 70cm² By cutting into a size, the final product containing 30g ketoprofen was obtained.

[0018]

[Example 2] The same operation as an example 1 was performed except having used the 1.5g propylene glycol instead of propylene-glycol monochrome laurate.

[Example 3] The same operation as an example 1 was performed except having used the 1.5g isopropyl myristate instead of propylene-glycol monochrome laurate.

[Example 4] The same operation as an example 1 was performed except having used 1.5g ethylene glycol monoethyl ether instead of propylene-glycol monochrome laurate.

[Example 5] The same operation as an example 1 was performed except having used the 14g polybutene instead of liquid paraffin.

[Example 6] The same operation as an example 1 was performed except having not used layer C.

[0019]

[Example(s) of Experiment] The endermic delivery system containing the ketoprofen manufactured in the aforementioned examples 1-6, and product of marketing as a contrast (ketoprofen delivery system plaster, keto top (KETOTOP)) Skin transmittance was measured

using the skin of a nude mouse, respectively. In this experiment, the skin was carried in the "Flow-through" diffusion cell using the nude mouse of about eight to 12 week-old. The product made into the method of a real trial was cut circularly, and was made to adhere to the skin so that the area may be set to 2 2cm. As a medium of a receiver cell, the phosphate buffer solution (pH7.4) was used and temperature was maintained at 37 degrees C. Samples are collected at the spacing of 2.5 hours for 20 hours, and it is high speed liquid chromatography (HPLC). After using and carrying out determination, the amount of medicine transparency by time was calculated. As a mobile phase of high speed liquid chromatography, methanol:water:phosphoric-acid (800:199:1) mixed liquor is used and it is a stationary phase. Zorbax Rx C8 It was used and measured by the 250nm ultraviolet region. At this time, an average of the penetrated amount of medicines is as the next table 1 per [in 12 hours to begin] unit time and per unit area.

[0020]

[Table 1]

mean skin transparency liquid of the ketoprofen measured among 12 hours of the start (mug / cm2/hr) *****
sample mean skin transmission rate (mug / cm2/hr) -----

----- The example 1 17.7 examples 2 16.8 Example 3 18.0
Example 4 15.1 examples 5 16.5 Example 6 15.8 Commercial-product 4.7

***** [0021] As shown in Table 1, since the nonpolar polymer is being used for the constituent for the endermic delivery system containing the non-steroidal anti-inflammatory drug of this invention as a basis polymer unlike the conventional product, it has the skin permeability superior to the commercial product. If it is that it is still required, as compared with the conventional product, the skin permeability of an active ingredient can be intentionally promoted by adding 1 or the component beyond it chosen out of the group which consists of a solubilizing agent, an absorption adjuvant, a **** agent, and a tackifier.

[0022]

[Effect of the Invention] In the case of the endermic delivery system which has a non-steroidal anti-inflammatory drug as an active ingredient by this invention as explained above The skin transparency effect is excellent by using a nonpolar polymeric material as a component of the macromolecule basis unlike the conventional product. Moreover, there is an effect which mixes and uses one or more components chosen from lysis aid and the absorption adjuvant, the **** agent, and the binder as an additive if needed, and increases the skin transmittance of an active ingredient remarkably compared with the former. The endermic delivery system of this invention is [in / the percutaneous absorption of the propionic-acid derivative which is one sort of a non-steroidal anti-inflammatory drug called ketoprofen] excellent in the physical characteristic again, and a good analgesic effect and the anti-inflammation effect are acquired.

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DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]

[Drawing 1] It is the cross section showing an example of the monolayer ***** type constituent of the endermic delivery system by this invention.

[Drawing 2] It is the cross section showing an example of the multilayer ***** type constituent of the endermic delivery system by this invention.

[Description of Notations]

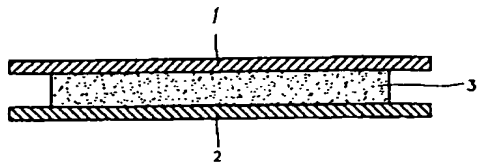
1, 11 *****

2, 12 Tooth-back layer

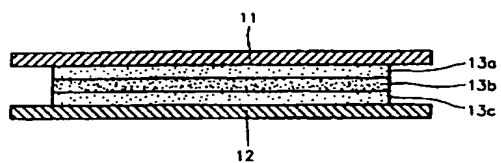
3, 13a, 13b, 13c Substrate layer

[Translation done.]

Drawing selection Drawing 1 ▼



[Translation done.]

Drawing selection Drawing 2 ▼

[Translation done.]